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(54) **MEASUREMENT APPARATUS, PROGRAM, AND MEASUREMENT METHOD**

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G01N 35/00 (2006.01)
G06T 7/20 (2006.01)

(52) **U.S. Cl.**
CPC ***G06T 7/0016*** (2013.01); ***G01N 35/0099*** (2013.01); ***G01N 35/00603*** (2013.01); ***G06T 7/20*** (2013.01); *G06T 2207/10056* (2013.01); *G06T 2207/30004* (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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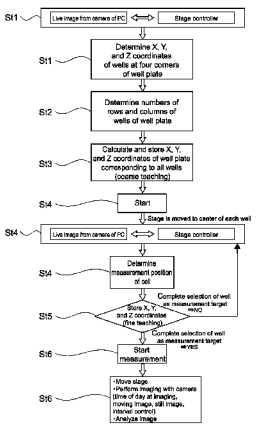
(57) **ABSTRACT**

There is provided a measurement apparatus including an objective lens, a stage, a setting unit, and a controller. The stage is configured to support a sample vessel in which a plurality of wells each containing a sample are arranged and to define relative positions of the sample vessel and the objective lens. The setting unit is configured to determine whether to set each of the plurality of wells to be a measurement target and set the measurement target. The controller is configured to control the stage such that a well determined to be the measurement target by the setting unit and the objective lens face each other.

14 Claims, 7 Drawing Sheets



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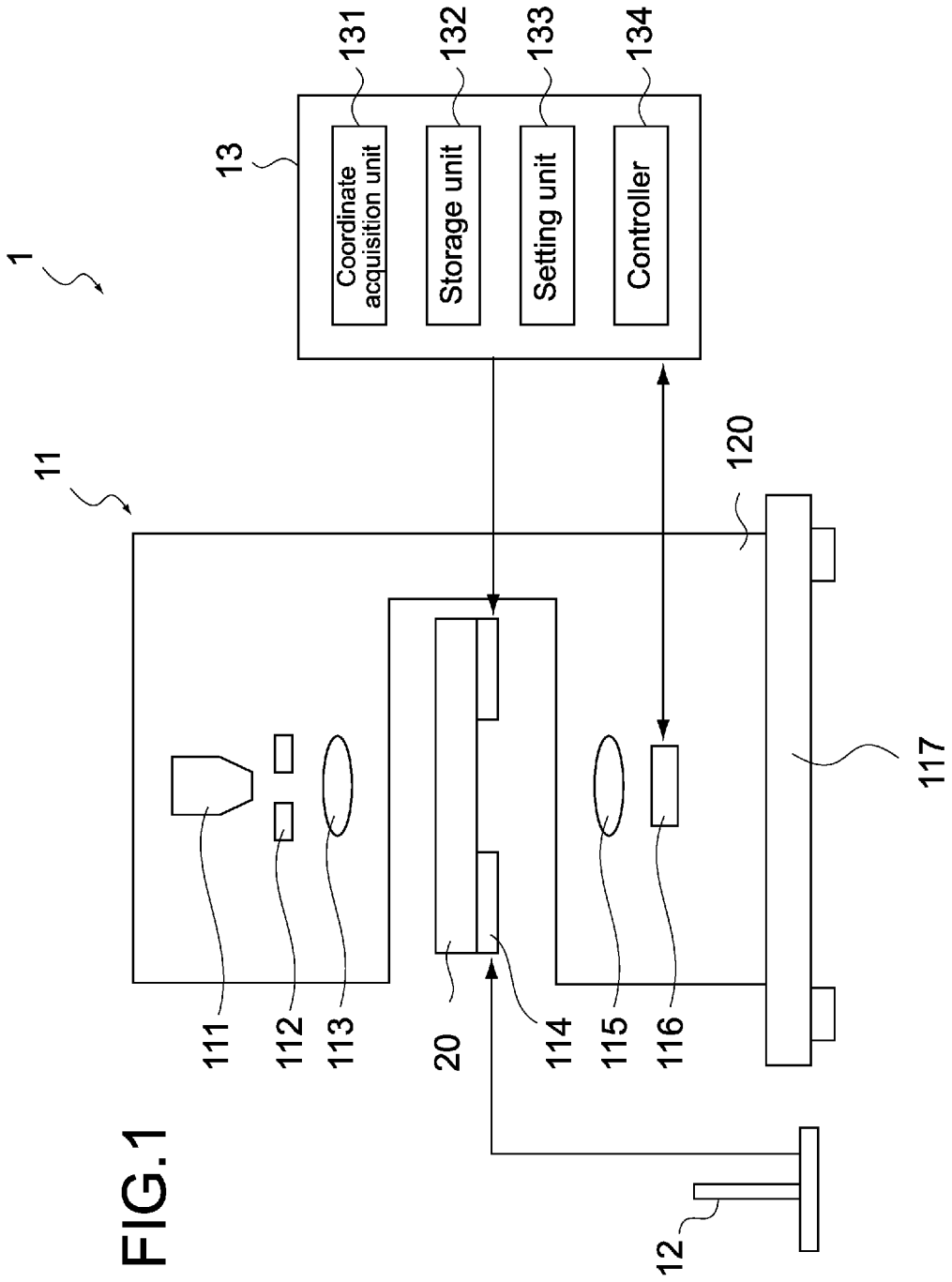
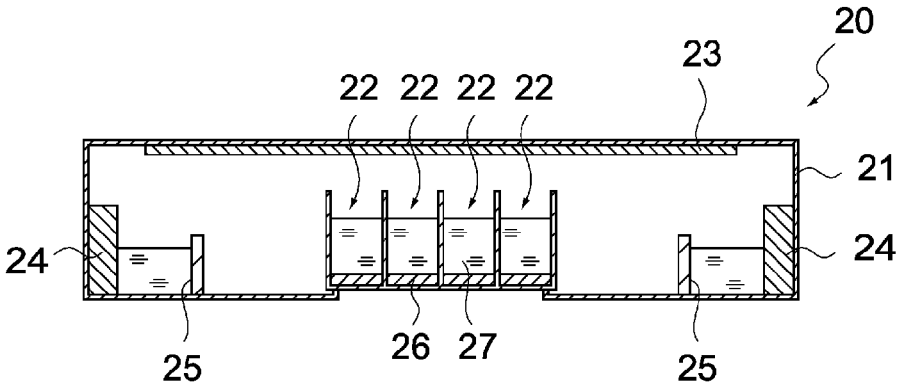

1
13
131
132
133
134
Coordinate acquisition unit
Storage unit
Setting unit
Controller
11
120
117
111
112
113
20
114
115
116
12

FIG.1

(a)



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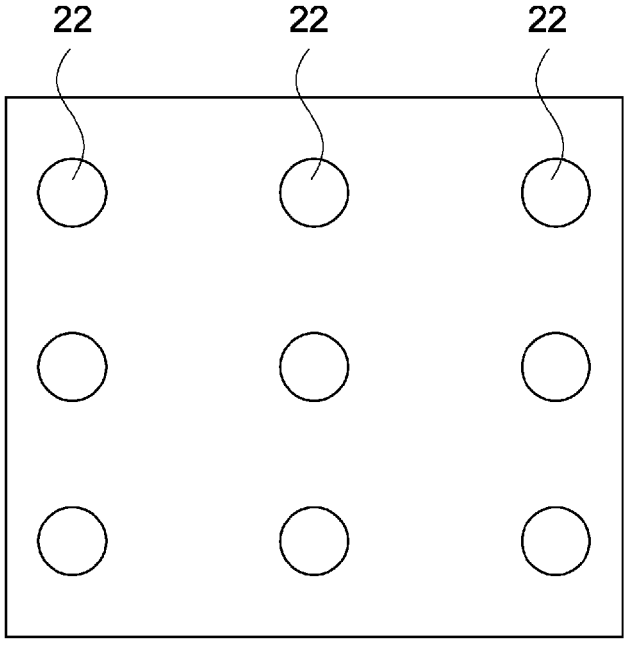
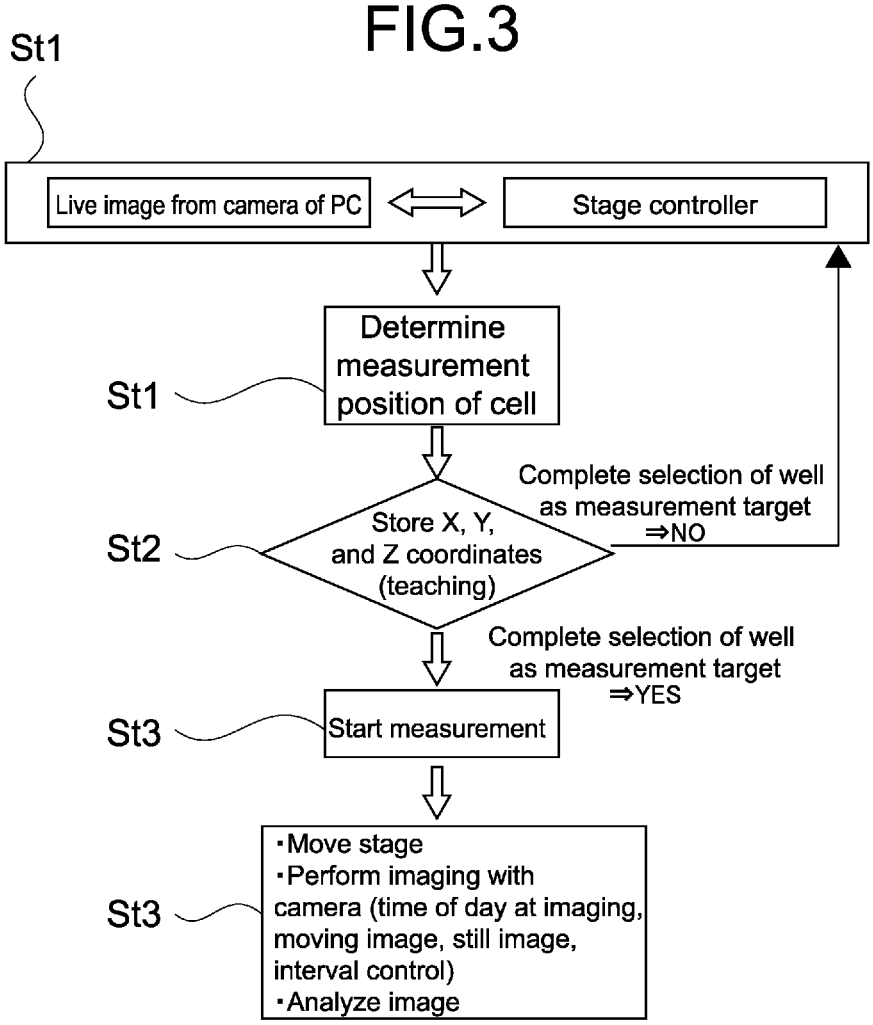


FIG.2

FIG.3


St1
Live image from camera of PC
Stage controller
Determine measurement position of cell
St1
Store X, Y, and Z coordinates (teaching)
St2
Complete selection of well as measurement target ⇒NO
Complete selection of well as measurement target ⇒YES
Start measurement
St3
・Move stage
・Perform imaging with camera (time of day at imaging, moving image, still image, interval control)
・Analyze image
St3

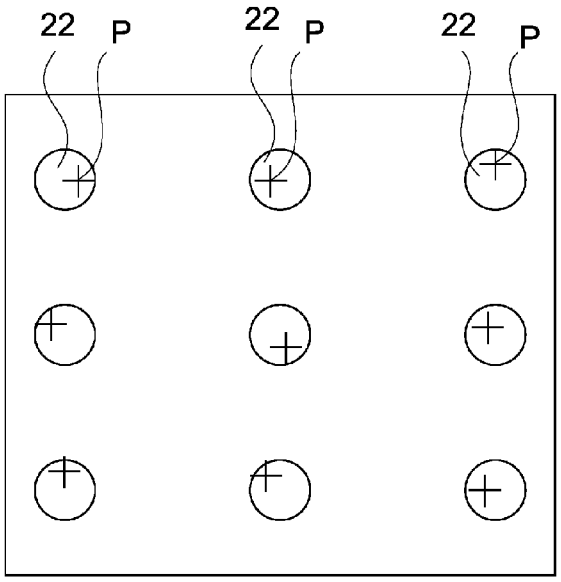
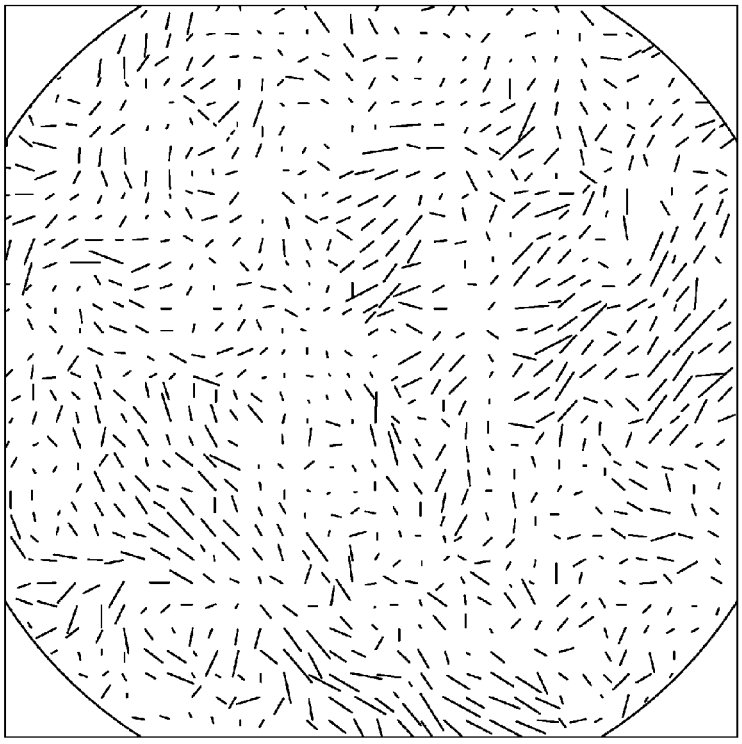


FIG.4

FIG.5



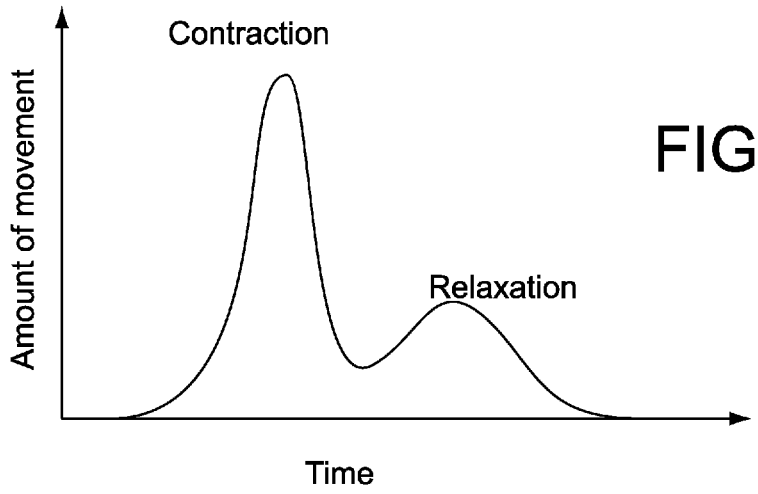


FIG.6

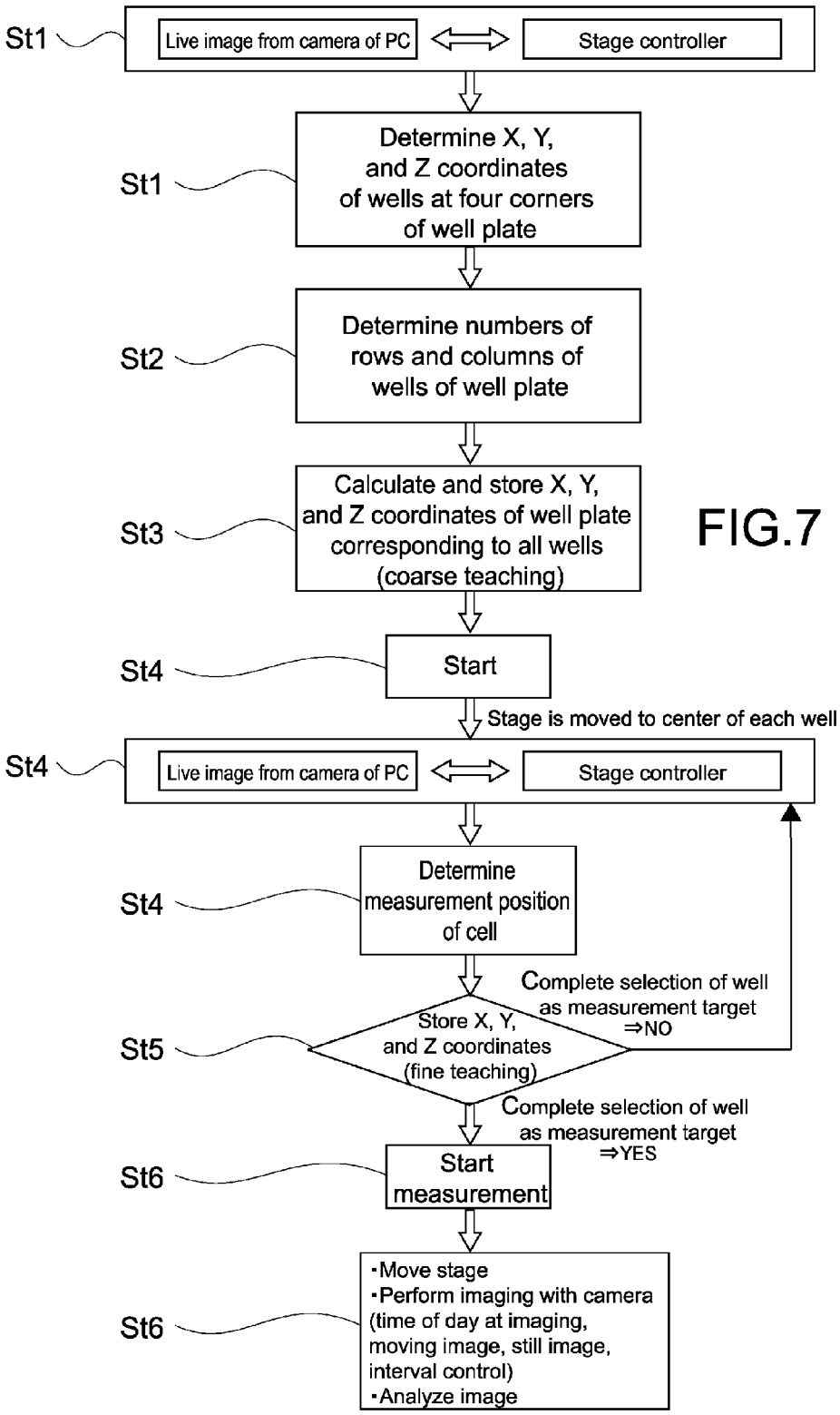

St1
Live image from camera of PC
Stage controller
St1
Determine X, Y, and Z coordinates of wells at four corners of well plate
St2
Determine numbers of rows and columns of wells of well plate
St3
Calculate and store X, Y, and Z coordinates of well plate corresponding to all wells (coarse teaching)
St4
Start
Stage is moved to center of each well
St4
Live image from camera of PC
Stage controller
St4
Determine measurement position of cell
St5
Store X, Y, and Z coordinates (fine teaching)
Complete selection of well as measurement target ⇒NO
Complete selection of well as measurement target ⇒YES
St6
Start measurement
St6
・Move stage
・Perform imaging with camera (time of day at imaging, moving image, still image, interval control)
・Analyze image

FIG.7

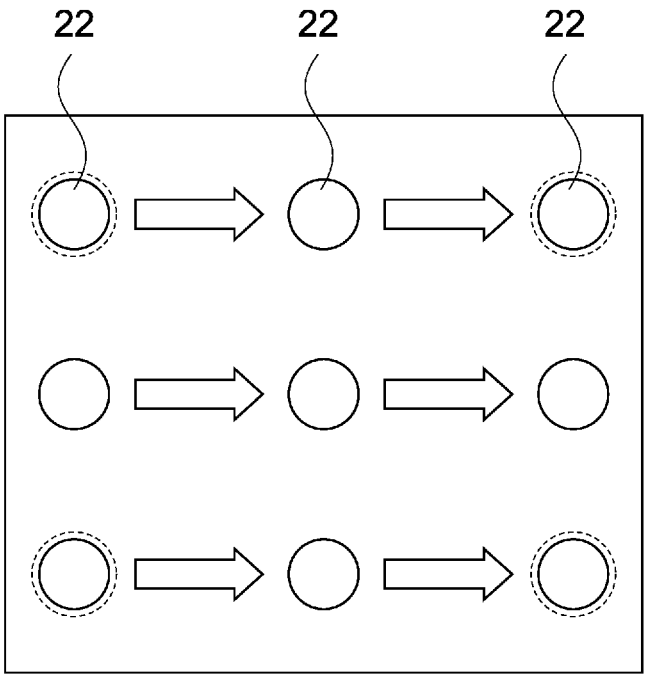


FIG.8

MEASUREMENT APPARATUS, PROGRAM, AND MEASUREMENT METHOD

CROSS REFERENCES TO RELATED APPLICATIONS

The present application is a national stage of International Application No. PCT/JP2013/000019 filed on Jan. 8, 2013 and claims priority to Japanese Patent Application No. 2012-005682 filed on Jan. 13, 2012, the disclosure of which is incorporated herein by reference.

BACKGROUND

The present disclosure relates to a measurement apparatus that measures samples contained in a plurality of wells by a microscope, and to a program and a measurement method therefor.

In the field of a pathological diagnosis and the like, in the case of measuring a sample that generates pulsations, such as a myocardial cell, image analysis may be performed on images of the sample magnified by a microscope. This is because the image analysis allows a movement of the sample to be observed with the elapse of time by comparing images captured at different times of day.

CITATION LIST

Patent Literature

[PTL 1]
Japanese Patent Application Laid-open No. 2008-289799
[PTL 2]
Japanese Patent Application Laid-open No. 2010-130966

SUMMARY

Technical Problem

Image analysis is performed on images of a sample magnified by a microscope to measure a sample that generates pulsations. For example, Patent Literature 1 discloses a cardiac function analyzing apparatus that analyzes a cardiac motion by image analysis. The cardiac function analyzing apparatus is configured to obtain the positions of anatomically corresponding points of a heart in images obtained by imaging the heart, thus calculating displacements of the points with the elapse of time. The cardiac function analyzing apparatus can display the movements of the respective points so as to meet the shape of the heart.

Further, Patent Literature 2 discloses a myocardial toxicity examining apparatus capable of performing image analysis in a laboratory system (in vitro system). The myocardial toxicity examining apparatus can evaluate the influence of a medicine on a myocardial cell by forming a cell network on a substrate, administering the medicine thereto, and detecting pulsations of a myocardial cell by image analysis.

As described above, the measurement apparatus that deals with a sample that generates pulsations, such as a myocardial cell, generally images the sample over a predetermined period of time (captures moving images or still images) to detect a movement of the sample based on the change of the images due to times of day. Therefore, it is necessary to eliminate vibrations of the measurement apparatus during measurement to extract only the change of the images due to pulsations.

A sample is generally contained in a section called well together with a culture solution. In general, a plurality of samples are measured collectively, and therefore a plurality of wells are provided. Here, there may be samples that are unsuitable for measurement among the samples contained in the plurality of wells. For example, such samples may be pulsatile cells whose pulsations are already stopped. The measurement of those wells is waste of time, and there arises a demand for improvement in such a case.

In view of the circumstances as described above, it is desirable to provide a measurement apparatus, a program, and a measurement method that are suitable for measurement of samples contained in a plurality of wells over a predetermined period of time by using a microscope.

Solution to Problem

According to an embodiment of the present disclosure, there is provided a measuring apparatus including a stage configured to support a vessel including a plurality of samples, each of the samples contained within a respective well. The measuring apparatus also includes an image device configured to capture an image of at least one sample and a processor communicatively coupled to a stage controller and configured to determine which of the plurality of samples are to be imaged and which of the plurality of samples are not to be imaged.

According to another embodiment of the present disclosure, there is provided a measurement apparatus including an objective lens, a stage, a setting unit, and a controller. The stage is configured to support a sample vessel in which a plurality of wells each containing a sample are arranged and to define relative positions of the sample vessel and the objective lens. The setting unit is configured to determine whether to set each of the plurality of wells to be a measurement target and set the measurement target. The controller is configured to control the stage such that a well determined to be the measurement target by the setting unit and the objective lens face each other.

With this configuration, the setting unit determines whether to set each of the plurality of wells to be a measurement target and sets the measurement target, with the result that the controller can control the stage so as to operate only for the well that has been determined to be the measurement target. Therefore, the measurement is not performed on wells that have not been determined to be measurement targets, which leads to the shortening of the whole measurement time.

The measurement apparatus may further include a coordinate acquisition unit configured to acquire coordinates of positions of the stage at which each of the plurality of wells faces the objective lens at an observation position thereof. The setting unit may be configured to supply, of the coordinates of the positions of the stage, coordinates of a position at which a well determined to be the measurement target faces the objective lens at an observation position thereof, to the controller.

With this configuration, the controller can move the stage to the coordinates of the position at which the well determined to be the measurement target and the objective lens face each other to thereby perform measurement.

The coordinate acquisition unit may be configured to acquire coordinates of positions of the stage at which each of the plurality of wells faces the objective lens at a center position thereof, and the controller may control the stage such that each of the plurality of wells faces the objective lens at the center position thereof.

With this configuration, since the stage is moved by the controller such that each of the plurality of wells faces the objective lens at the center position thereof, it is not necessary to adjust the position of the stage such that each well falls within the field of view when the user determines an observation position of an image of each well. Therefore, the user can determine the observation position speedily, which leads to the shortening of the whole measurement time.

The coordinate acquisition unit may be configured to acquire, based on coordinates of positions of the stage at which each of wells at four corners of the sample vessel faces the objective lens at a center position thereof, the wells being designated by a user, and on an array of the plurality of wells in the sample vessel, the coordinates of the positions of the stage at which each of the plurality of wells faces the objective lens at the center position thereof.

The setting unit may be configured to perform the setting based on a result of image analysis of the sample, the result being imaged via the objective lens.

With this configuration, it is possible to automatically determine a well that is not determined to be a measurement target by the setting unit based on the result of the image analysis of the sample, for example, on the level of the pulsations of the sample.

The sample may include a pulsatile cell, and the setting unit may be configured to exclude, from measurement targets, a well containing a pulsatile cell whose pulsations are stopped.

As described above, when the pulsatile cell is used as a sample to measure its pulsations, it is not necessary to measure a sample whose pulsations are stopped. With this configuration, a sample whose pulsations are already stopped can be prevented from being measured.

The measurement apparatus may further include a vibration isolation table including the objective lens and the stage and being configured to attenuate vibrations from the outside.

With this configuration, it is possible to remove, by the vibration isolation table, vibrations applied to the measurement apparatus from the outside and prevent the reduction in measurement precision due to the influence of the vibrations when the pulsations of a cell is measured over a predetermined period of time.

According to another embodiment of the present disclosure, there is provided a program causing a computer to function as a setting unit and a controller. The setting unit is configured to determine whether to set each of a plurality of wells to be a measurement target and set the measurement target in a sample vessel in which the plurality of wells each containing a sample are arranged. The controller is configured to control a stage configured to support the sample vessel such that a well determined to be the measurement target by the setting unit and an objective lens face each other.

According to another embodiment of the present disclosure, there is provided a measurement method including: determining, by a setting unit, whether to set each of a plurality of wells to be a measurement target and setting the measurement target in a sample vessel in which the plurality of wells each containing a sample are arranged; and controlling, by a controller, a stage configured to support the sample vessel such that a well determined to be the measurement target by the setting unit and an objective lens face each other.

Advantageous Effect of Invention

As described above, according to the embodiments of the present disclosure, it is possible to provide a measurement apparatus, a program, and a measurement method that are suitable for measurement of samples contained in a plurality of wells over a predetermined period of time by using a microscope.

Additional features and advantages are described herein, and will be apparent from the following Detailed Description and the figures.

BRIEF DESCRIPTION OF THE FIGURES

FIG. **1** is a schematic diagram showing the configuration of a measurement apparatus according to a first embodiment and a second embodiment.

FIGS. **2**A and **2**B are schematic views each showing the configuration of a culture vessel mounted to the measurement apparatus.

FIG. **3** is a flowchart showing the operation of the measurement apparatus according to the first embodiment.

FIG. **4** is a schematic diagram showing an observation position in each well.

FIG. **5** is a diagram showing an example of results of image analysis performed by the measurement apparatus.

FIG. **6** is a graph as an example obtained based on the results of the image analysis performed by the measurement apparatus.

FIG. **7** is a flowchart showing the operation of the measurement apparatus according to the second embodiment.

FIG. **8** is a schematic diagram showing the movement control of a stage.

DETAILED DESCRIPTION

(First Embodiment)

Hereinafter, a measurement apparatus according to a first embodiment will be described.

(Configuration of Measurement Apparatus)

FIG. **1** is a schematic diagram showing the configuration of a measurement apparatus **1**. As shown in FIG. **1**, the measurement apparatus **1** includes a main body **11**, a stage controller **12**, and a PC (Personal Computer) **13**. The main body **11** may be a phase-contrast microscope. It should be noted that such a configuration is merely an example, and the configuration corresponding to the stage controller **12** and the PC **13** may be provided to the main body **11**.

In the main body **11**, the casing **120** houses an illumination light source **111**, a ring aperture **112**, a condenser lens **113**, a stage **114**, an objective lens **115**, and an imaging device **116** and is mounted on a vibration isolation table **117**. The culture vessel **20** in which a sample is contained is mounted on the stage **114**.

The illumination light source **111** is a light source that irradiates the culture vessel **20** with illumination light, for example, visible light or excitation light. The illumination light source **111** may be an LED (Light Emitting Diode) and the like. The ring aperture **112** is an aperture for adjusting the amount of illumination light emitted from the illumination light source **111**. The condenser lens **113** is a lens for condensing the illumination light having passed through the ring aperture **112** to the culture vessel **20**. The configuration of the illumination light source **111**, the ring aperture **112**, and the condenser lens **113** may be changed as appropriate.

The stage **114** supports the culture vessel **20** and defines relative positions of the culture vessel **20** and the objective lens **115**. Specifically, the stage **114** is configured to be three-dimensionally movable with respect to the casing **120** provided with the objective lens **115** and is movable on an

X-Y plane (plane parallel to a mounting surface of the stage) and in a Z direction (direction vertical to the mounting surface of the stage). The stage **114** is connected to the stage controller **12** and is configured to move in accordance with the operation of the stage controller **12** by the user.

The objective lens **115** magnifies the light having been emitted from the illumination light source **111** and having passed through the sample at a predetermined magnification, and condenses the light to the imaging device **116**. The objective lens **115** may be, for example, an objective lens incorporating a phase difference ring. The imaging device **116** is an imaging device capable of capturing a moving image and may be a CCD (Charge Coupled Device), a CMOS (Complementary Metal Oxide Semiconductor), and the like. The imaging device **116** is connected to the PC **13** and is configured to output a captured image (moving image) to the PC **13**.

The vibration isolation table **117** supports the casing **120** and attenuates vibrations of an outer portion (mounting surface). A vibration isolation table for a microscope that is capable of coping with micro vibrations is suitable for the vibration isolation table **117**. The main body **11** has the configuration as described above. The main body **11** may have an alternate or additional configuration in addition to the configurations used herein and may include an eyepiece lens, for example.

The culture vessel **20** can have a plurality of wells (sections in which samples are contained) arranged along the X-Y plane. FIG. **2** are schematic views each showing the culture vessel **20**. FIG. **2**A is a cross-sectional view of the culture vessel **20**, and FIG. **2**B is a plan view of the culture vessel **20**.

As shown in FIG. **2**A, the culture vessel **20** includes a culture chamber **21**, wells **22**, a glass heater **23**, heaters **24**, and a tank **25**. Each of the wells **22** contains a sample **26** and a culture solution **27**.

The culture chamber **21** is a chamber capable of keeping its inside airtight and houses the wells **22**, the glass heater **23**, the heaters **24**, and the tank **25**. Each of the wells **22** is a section partitioned by partition walls and capable of retaining liquid. As shown in FIG. **2**B, a plurality of wells **22** are arranged in a matrix. FIGS. **2**A and **2**B show a small number of wells **22**, but a larger number of wells **22**, for example, 96 wells **22** or **48** wells **22** are provided in reality.

The glass heater **23** and the heaters **24** are heaters for keeping predetermined temperature, for example, temperature suitable for the cultivation of cells, in the culture chamber **21**. The glass heater **23** has light transparency in order to transmit illumination light. The tank **25** is provided on the inner circumference of the culture chamber **21** and is configured to retain water used for keeping predetermined humidity in the culture chamber **21**.

The samples **26** are contained in the respective wells **22**. Though not particularly limited, the samples **26** may be pulsatile cells, for example, myocardial cells. The culture solution **27** is for cultivating the samples **26** and is appropriately selected in accordance with the types of samples **26**.

The culture chamber **21** can be filled with a cultivation gas suitable for cultivation of the samples **26**. The cultivation gas may be, for example, air having a temperature of 37° C. and containing 5 to 7% of CO_2.

The culture vessel **20** can be configured as described above. The illumination light coming from the condenser lens **113** passes through the culture chamber **21** and the glass heater **23** and enters one of the wells **22**. The illumination light passes through the culture solution **27** and the sample **26** and is emitted from the bottom surface of the well **22** to reach the objective lens **115**. The replacement of the sample **26** and the culture solution **27** can be performed by removing the glass heater **23**.

The stage controller **12** is connected to the stage **114** and is configured to move the stage **114** in the X-Y plane direction and in the Z direction upon reception of an operation by the user. Any stage controller may be used as the stage controller **12**.

The PC **13** is constructed by cooperation of software and hardware such as a processor, a memory, and storage and may have the configuration as shown in FIG. **1**. Specifically, the PC **13** includes a coordinate acquisition unit **131**, a storage unit **132**, a setting unit **133**, and a controller **134**.

The coordinate acquisition unit **131** acquires coordinates of the stage **114**. Specifically, when the user operates the stage controller **12** to move the stage **114** to coordinates of a predetermined position (hereinafter, referred to also as position coordinates), the coordinate acquisition unit **131** receives an instruction of the user to acquire the position coordinates of the stage **114** at that time. The position coordinates of the stage **114** can be acquired as, for example, numerical values of X, Y, and Z coordinates.

The storage unit **132** stores the position coordinates of the stage **114**, which have been acquired by the coordinate acquisition unit **131**. The storage unit **132** supplies the position coordinates to the controller **134** in response to a request.

The setting unit **133** determines whether to set each of the plurality of wells **22** to be a measurement target and set the measurement target. The setting unit **133** determines a well **22** unsuitable for measurement by means of the designation by the user, the analysis of captured images (to be described later), or the measurement using electrodes (to be described later). For example, in the case where the sample **26** is a pulsatile cell, the well **22** unsuitable for measurement may be a well **22** containing a pulsatile cell whose pulsations are stopped. Further, the setting unit **23** can set, of the wells **22**, the well **22** located at the outer circumference to be a well unsuitable for measurement. This is because the culture solution **27** evaporates faster in the well **22** located at the outer circumference than in the other wells **22**.

The controller **134** moves the stage **114** to be located at the position coordinates stored in the storage unit **132** and causes the imaging device **116** to capture an image of the sample **26** (moving image or continuous still images). Upon completion of the imaging, the controller **134** moves the stage **114** to the next position coordinates and causes the imaging device **116** to perform imaging in a repeated manner. In the case where a well **22** that is not determined to be a measurement target is set by the setting unit **133**, the controller **134** does not move the stage **114** to position coordinates corresponding to the well **22** and moves the stage **114** to position coordinates of another well **22** as the next measurement target.

The PC **13** may be configured as described above. In addition thereto, it is assumed that the PC **13** is connected with an input interface, a display, and the like (not shown).

(Operation of Measurement Apparatus)

The operation of the measurement apparatus **1** configured as described above will be described. FIG. **3** is a flowchart showing the operation of the measurement apparatus **1**.

First, the user determines an observation position (St **1**). Specifically, the user operates the stage controller **12** while viewing a low-magnification image of a partial area in the culture vessel **20**, which is displayed on the display of the PC **13**, and focuses the field of view on one of the wells **22**. Next, the well **22** is magnified and the observation position

in the well **22** is determined. For example, in the case where the sample **26** is a pulsatile cell, the observation position may be set to a position where active pulsations are observed. FIG. **4** is a schematic diagram showing an example of observation positions in the respective wells **22** of the culture vessel **20** (observation positions being denoted by P in FIG. **4**).

Upon determination of the observation position, the user makes inputs to the PC **13**. In response to this, the coordinate acquisition unit **131** acquires position coordinates of the stage **114** at that time and supplies the position coordinates to the storage unit **132** (teaching) (St **2**). Subsequently, the user returns the magnification of the image to a lower one and focuses the field of view on the next well **22**. Further, the user determines the observation position in the well **22** in the above-mentioned manner and makes inputs to the PC **13**. The coordinate acquisition unit **131** acquires position coordinates of the stage **114** at that time in the same manner. After that, the user designates an observation position of each of the wells **22** in the same manner so that the coordinate acquisition unit **131** acquires position coordinates of the stage **114** for each of the wells **22**.

Here, in the case where there are wells **22** unsuitable for measurement, such as a well **22** containing a pulsatile cell whose pulsations are stopped, the user can make inputs indicating that the wells **22** are unsuitable for measurement to the PC **13**. In response to this, the setting unit **133** can delete the position coordinates corresponding to the wells **22** from the storage unit **132**. Further, the setting unit **133** can detect the wells **22** unsuitable for measurement based on results of the image analysis to be described later or the output of electrodes immersed in the wells **22** in addition to the inputs by the user and delete the position coordinates of the wells **22** from the storage unit **132**.

Upon completion of the determination of the observation positions for all the wells **22** in the culture vessel **20**, the measurement is started (St **3**). The controller **134** acquires the position coordinates of the stage **114**, which correspond to the wells **22**, from the storage unit **132** and moves the stage **114** so as to be positioned at the position coordinates. Upon completion of the movement of the stage **114**, the controller **134** causes the imaging device **116** to capture an image (moving image or still image). In this case, the controller **134** may control the illumination light source **111**, the ring aperture **112**, and the objective lens **115** at the same time and adjust imaging conditions.

Upon completion of the movement of the stage **114** and the imaging by the imaging device **116** for all the position coordinates stored in the storage unit **132**, this measurement is terminated. After that, for example, it is also possible to perform the movement of the stage **114** and the imaging by the imaging device **116** again after the elapse of several hours and perform the measurement of the sample **26** over several days.

The image of the sample **26** captured by the imaging device **116** (hereinafter, captured image) is subjected to image analysis by image analysis software of the PC **13**. Hereinafter, the image analysis will be described. FIG. **5** is a diagram showing an example of results of analysis. The image analysis may be, for example, motion detection processing by block matching and detect how much a point set in an image is moved within a predetermined period of time by block matching.

In the image shown in FIG. **5**, the length of a line corresponds to a vector of a movement. This signal is integrated in a target portion to be analyzed, thus obtaining signals of contraction, relaxation, and the like. FIG. **6** is a graph showing the amount of the movement with respect to the time, which has been obtained by the analysis.

When the well **22** unsuitable for measurement is subjected to determination, the results of the image analysis may be used. Specifically, after the imaging performed by the imaging device **116**, if the total amount of the movement obtained based on the result of the image analysis for the captured image has a predetermined threshold value or smaller, it can be determined that the pulsations of the sample **26** contained in the well **22** are stopped. In subsequent measurement, the controller **134** can exclude the well **22** from measurement targets.

As described above, in this embodiment, a well **22** unsuitable for measurement is set by the setting unit **133** so that the well **22** does not face the objective lens **115** when the controller **134** controls the stage. Thus, the well **22** unsuitable for measurement is prevented from being imaged by the imaging device **116**, and a measurement time can be shortened. Further, since the vibration isolation table **117** prevents vibrations from the outside from being transmitted, the influence due to the vibrations at a time of image analysis is eliminated so that precise analysis can be performed.

(Second Embodiment)

Hereinafter, a measurement apparatus according to a second embodiment will be described. Since the measurement apparatus according to this embodiment has the same configuration as that of the measurement apparatus **1** according to the first embodiment, the description thereof will be omitted.

(Operation of Measurement Apparatus)

The operation of the measurement apparatus **1** according to this embodiment will be described. FIG. **7** is a flowchart showing the operation of the measurement apparatus **1**. In this embodiment, the operation of determining the positions of the wells **22** in the culture vessel **20** will be executed before the operation of the measurement apparatus **1** described in the first embodiment.

First, a user designates wells **22** at four corners of the culture vessel **20** (St **1**). Specifically, the user operates the stage controller **12** while viewing a low-magnification image of a partial area in the culture vessel **20**, which is displayed on the display of the PC **13**, and focuses the field of view on one of the wells **22** located at the four corners, thus making inputs to the PC **13**.

In response to this, the coordinate acquisition unit **131** acquires the position coordinates of the stage **114** at that time and causes the storage unit **132** to store the position coordinates. Similarly, when the user designates the wells **22** at the four corners, the storage unit **132** stores the position of the stage **114** at that time.

Next, the user inputs the array of the wells **22** in the culture vessel **20** (St **2**). For example, the numbers of rows and columns of the array of the wells **22** may be input. The coordinate acquisition unit **131** calculates the positions of all the wells **22** in the culture vessel **20** based on position coordinates of the stage **114** that correspond to the wells **22** at the four corners and the array of the wells **22**, and the storage unit **132** stores the position coordinates of the stage **114** at which each of the wells **22** falls within the field of view (coarse teaching) (St **3**).

After that, the user determines an observation position in each of the wells **22** as in the first embodiment (St **4** to St **6**). Here, in this embodiment, since the stage position corresponding to each of the wells **22** are stored in advance in the storage unit **132** as described above, the automatic positioning of the stage **114** is performed as follows.

FIG. **8** is a schematic diagram showing the operation of the automatic positioning of the stage **114** by the controller **134**. As shown in FIG. **8**, when the user makes inputs to the PC **13**, the controller **134** moves the stage **114** to the position coordinates stored in the storage unit **132** (movement path is indicated by arrows in FIG. **8**). Thus, the user does not need to focus the field of view of the images on one of the wells **22** by using the stage controller **12** while viewing a low-magnification image and can determine the observation position.

When the user makes inputs to the PC **13** again after determining the observation position, the controller **134** moves the stage **114** to the position coordinates corresponding to the next well **22** and being stored in the storage unit **132**. Specifically, the user does not need to set the field of view of the images at a lower magnification to search for the next well **22** and can determine the observation position without changing the high magnification of the images.

Thus, the observation positions of all the wells **22** in the culture vessel **20** are determined (St **4**). The coordinate acquisition unit **131** acquires the position coordinates of the stage **114** at the respective observation positions and supplies the position coordinates to the storage unit **132** (fine teaching) (St **5**). In the case where there are wells **22** unsuitable for measurement as in the first embodiment, the user can make inputs indicating that the wells **22** are unsuitable for measurement to the PC **13**. In response to this, the setting unit **133** can delete the position coordinates corresponding to the wells **22** from the storage unit **132**. Further, the setting unit **133** can detect the wells **22** unsuitable for measurement based on results of the image analysis or the output of electrodes immersed in the wells **22** in addition to the inputs by the user and delete the position coordinates of the wells **22** from the storage unit **132**.

Upon completion of the determination of the observation positions for all the wells **22** in the culture vessel **20**, the measurement is started (St **6**). The controller **134** acquires the position coordinates of the stage **114**, which correspond to the wells **22**, from the storage unit **132** and moves the stage **114** so as to be positioned at the position coordinates. Upon completion of the movement of the stage **114**, the controller **134** causes the imaging device **116** to capture an image (moving image or still image). In this case, the controller **134** may control the illumination light source **111**, the ring aperture **112**, and the objective lens **115** at the same time and adjust imaging conditions.

Upon completion of the movement of the stage **114** and the imaging by the imaging device **116** for all the position coordinates stored in the storage unit **132**, this measurement is terminated. After that, for example, it is also possible to perform the movement of the stage **114** and the imaging by the imaging device **116** again after the elapse of several hours and perform the measurement of the sample **26** over several days.

Upon completion of the determination of the observation positions for all the wells **22** in the culture vessel **20**, the measurement is started. The controller **134** acquires the position coordinates of the stage **114**, which correspond to the wells **22**, from the storage unit **132** and moves the stage **114** so as to be positioned at the position coordinates. Upon completion of the movement of the stage **114**, the controller **134** causes the imaging device **116** to capture an image (moving image or still image). After that, the movement of the stage **114** and the imaging by the imaging device **116** are repeatedly performed. As in the first embodiment, the image analysis can be performed on a captured image.

As described above, in this embodiment, a well **22** unsuitable for measurement is set by the setting unit **133** so that the well **22** does not face the objective lens **115** when the controller **134** controls the stage. Thus, the well **22** unsuitable for measurement is prevented from being imaged by the imaging device **116**, and a measurement time can be shortened. Further, since the vibration isolation table **117** prevents vibrations from the outside from being transmitted, the influence due to the vibrations at a time of image analysis is eliminated so that precise analysis can be performed.

Further, in this embodiment, the position coordinates of the stage **114** at which each of the wells **22** falls within the field of view are acquired in advance so that the position coordinates of the stage **114** are automatically controlled when the user determines an observation position in each of the wells **22**. Thus, the user does not need to perform an operation of focusing the field of view on each of the wells, which increases convenience of the user.

The present disclosure is not limited to the embodiments described above and can be modified without departing from the gist of the present disclosure.

It should be noted that the present disclosure can employ the following configurations.

(1) A measurement apparatus, including:
an objective lens;
a stage configured to support a sample vessel in which a plurality of wells each containing a sample are arranged and to define relative positions of the sample vessel and the objective lens;
a setting unit configured to determine whether to set each of the plurality of wells to be a measurement target and set the measurement target; and
a controller configured to control the stage such that a well determined to be the measurement target by the setting unit and the objective lens face each other.

(2) The measurement apparatus according to (1), further including a coordinate acquisition unit configured to acquire coordinates of positions of the stage at which each of the plurality of wells faces the objective lens at an observation position thereof, in which
the setting unit is configured to supply, of the coordinates of the positions of the stage, coordinates of a position at which a well determined to be the measurement target faces the objective lens at an observation position thereof, to the controller.

(3) The measurement apparatus according to (1) or (2), in which
the coordinate acquisition unit is configured to acquire coordinates of positions of the stage at which each of the plurality of wells faces the objective lens at a center position thereof, and
the controller controls the stage such that each of the plurality of wells faces the objective lens at the center position thereof.

(4) The measurement apparatus according to any one of (1) to (3), in which
the coordinate acquisition unit is configured to acquire, based on coordinates of positions of the stage at which each of wells at four corners of the sample vessel faces the objective lens at a center position thereof, the wells being designated by a user, and on an array of the plurality of wells in the sample vessel, the coordinates of the positions of the stage at which each of the plurality of wells faces the objective lens at the center position thereof.

(5) The measurement apparatus according to any one of (1) to (4), in which

the setting unit is configured to perform the setting based on a result of image analysis of the sample, the result being imaged via the objective lens.

(6) The measurement apparatus according to any one of (1) to (5), in which

the sample includes a pulsatile cell, and

the setting unit is configured to exclude, from measurement targets, a well containing a pulsatile cell whose pulsations are stopped.

(7) The measurement apparatus according to any one of (1) to (6), further including a vibration isolation table including the objective lens and the stage and being configured to attenuate vibrations from the outside.

(8) A program causing a computer to function as:

a setting unit configured to determine whether to set each of a plurality of wells to be a measurement target and set the measurement target in a sample vessel in which the plurality of wells each containing a sample are arranged; and

a controller configured to control a stage configured to support the sample vessel such that a well determined to be the measurement target by the setting unit and an objective lens face each other.

(9) A measurement method, comprising:

determining, by a setting unit, whether to set each of a plurality of wells to be a measurement target and setting the measurement target in a sample vessel in which the plurality of wells each containing a sample are arranged; and

controlling, by a controller, a stage configured to support the sample vessel such that a well determined to be the measurement target by the setting unit and an objective lens face each other.

(10) A measuring apparatus comprising:

a stage configured to support a vessel including a plurality of samples, each of the samples contained within a respective well;

an image device configured to capture an image of at least one sample; and

a processor communicatively coupled to a stage controller and configured to determine which of the plurality of samples are to be imaged by the image device.

(11) The measuring apparatus according to (10), wherein the processor is configured to determine which of the plurality of samples are not to be imaged.

(12) The measuring apparatus according to of any one of (10) or (11), wherein the processor is configured to provide instructions causing the stage controller to move the stage or the image device to align the image device with the at least one sample that has been determined to be imaged.

(13) The measuring apparatus according to of any one of (10) to (12), wherein the processor is configured to determine which of the plurality of samples is to be imaged based on image analysis.

(14) The measuring apparatus according to of any one of (10) to (13), wherein the processor is configured to perform the image analysis by:

determining an amount of movement of the sample within the respective well by comparing previous images of the sample in the well; and

determining the sample is not to be further imaged if the amount of movement is below a predetermined threshold.

(15) The measuring apparatus according to of any one of (10) to (14), wherein the processor is configured to determine a location for each of the plurality of samples on the vessel by:

prompting a user to align a least one well with the image device;

determining an observation position within each well; and

recording the location relative to the vessel of each of the observation positions aligned with the image device.

(16) The measuring apparatus according to of any one of (10) to (15), wherein the processor is configured to determine the location for each of the plurality of samples on the vessel by:

prompting the user for a number of rows and columns of the wells included within the vessel; and

determining the locations of each of the samples based on the known locations of wells aligned with the image device and the number of rows and columns of the vessel.

(17) The measuring apparatus according to of any one of (10) to (16), wherein the processor is configured to prompt the user to align the wells located on four corners of the vessel with the image device.

(18) The measuring apparatus according to of any one of (10) to (17), wherein the processor is configured to:

determine the observation position for each of the plurality of samples by detecting within each well where the sample is visually active; and

control movement of the stage to align each sample with the image device based on the determined observation position.

(19) The measuring apparatus according to of any one of (10) to (18), wherein at least one of the wells includes two samples and the processor is configured to determine the observation point by determining which of the two samples is more visually active.

(20) The measuring apparatus according to of any one of (10) to (19), wherein the processor is configured to determine that the well has two observation points when both of the samples included within a well have a visual activity that is greater than a predetermined threshold.

(21) The measuring apparatus according to of any one of (10) to (20), wherein the processor is configured to determine which of the plurality of samples is to be imaged based on an input from a user.

(22) The measuring apparatus according to of any one of (10) to (21), further comprising a vibration isolation table configured to prevent vibrations external to the measuring apparatus from being transmitted to at least one of the stage or the image device.

(23) A method of measuring at least one sample included within respective wells of a vessel, the method comprising:

determining an observation position for each of the plurality of samples;

determining which of the plurality of samples is to be imaged by an image device; and

imaging the samples determined to be imaged using the image device.

(24) The method according to (23), further comprising:

determining which of the plurality of samples is not to be imaged by the image device; and

refraining from imaging the samples that are not to be imaged.

(25) The method according to any one of (23) or (24), wherein determining the observation positions includes:

determining coordinates of wells at four corners of the vessel;

determining a number of rows and columns of wells within the vessel;

calculating coordinates for each of the wells based on the known locations of the wells at the four corners and the number of rows and columns of the vessel; and

identifying a portion of each well as the observation position where the respective sample is visually active above a predetermined threshold.

(26) The method according to any one of (23) to (25), wherein the coordinates of the wells at the four corners and the number of rows and columns is provided by a user responsive to a prompt.

(27) The method according to any one of (23) to (26), wherein determining which if the plurality of samples to be imaged includes:

determining at least one movement vector from portions of the sample within the respective well by comparing previous images of the portions of sample in the well; and

determining the sample is not to be further imaged if an average of the at least one movement vector for each of the portions is below a predetermined threshold.

(28) The method according to any one of (23) to (27), wherein determining which if the plurality of samples to be imaged includes receiving an indication from a user.

(29) The method according to any one of (23) to (28), further comprising moving a stage holding the vessel or the image device to align the image device with the at least one sample that has been determined to be imaged.

(30) A machine-accessible medium having instructions stored thereon that are configured when executed to cause a machine to at least:

determine an observation position for each of a plurality of samples included within respective wells of a vessel;

determine which of the plurality of samples is to be imaged by an image device; and

image the samples determined to be imaged using the image device.

(31) The machine-accessible medium according to (30), wherein the observation position includes coordinates relative to the vessel that correspond to which sample is to be aligned with the image device.

(32) The machine-accessible medium according to any one of (30) or (31), further comprising instructions stored thereon that are configured when executed to cause a machine to at least:

determine an amount of activity of the sample within each of the wells by comparing previous images of the sample in the well; and

determining the sample is not to be further imaged if the amount of activity is below a predetermined threshold.

(33) The machine-accessible medium according to any one of (30) to (32), further comprising instructions stored thereon that are configured when executed to cause a machine to at least move a stage holding the vessel or the image device to align the image device with the at least one sample that has been determined to be imaged.

(34) The machine-accessible medium according to any one of (30) to (33), further comprising instructions stored thereon that are configured when executed to cause a machine to at least image one sample at a time.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present subject matter and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

REFERENCE SIGNS LIST

11 main body
12 stage controller
13 PC
20 culture vessel
22 well
22 all wells
114 stage
115 objective lens
117 vibration isolation table
131 coordinate acquisition unit
132 storage unit
133 setting unit
134 controller

The invention claimed is:

1. A measuring apparatus comprising:

a stage configured to support a vessel including a plurality of samples, each of the samples contained within a respective well of a plurality of wells;

an image device configured to capture an image of at least one sample; and

a processor communicatively coupled to a stage controller and configured to determine which of the plurality of samples are to be imaged by the image device, based on image analysis of determining an amount of movement of the sample within the respective well by comparing previous images of the sample in the well, and determining the sample is not to be further imaged if the amount of movement is below a predetermined threshold,

wherein at least one of the plurality of wells includes two samples and the processor is configured to determine an observation position by determining which of the two samples is more visually active.

2. The measuring apparatus of claim **1**, wherein the processor is configured to determine a location for each of the plurality of samples on the vessel by:

prompting a user to align the at least one of the plurality of wells with the image device;

determining the observation position within each well; and

recording the location relative to the vessel of each of the observation positions aligned with the image device.

3. The measuring apparatus of claim **2**, wherein the processor is configured to determine the location for each of the plurality of samples on the vessel by:

prompting the user for a number of rows and columns of the wells included within the vessel; and

determining the locations of each of the samples based on the known locations of wells aligned with the image device and the number of rows and columns of the vessel.

4. The measuring apparatus of claim **2**, wherein the processor is configured to prompt the user to align the wells located on four corners of the vessel with the image device.

5. The measuring apparatus of claim **2**, wherein the processor is configured to:

determine the observation position for each of the plurality of samples by detecting within each well where the sample is visually active; and

control movement of the stage to align each sample with the image device based on the determined observation position.

6. A measuring apparatus comprising:

a stage configured to support a vessel including a plurality of samples, each of the samples contained within a respective well of a plurality of wells;

an image device configured to capture an image of at least one sample; and

a processor communicatively coupled to a stage controller and configured to determine which of the plurality of samples are to be imaged by the image device, based on image analysis of determining an amount of movement of the sample within the respective well by comparing previous images of the sample in the well, and determining the sample is not to be further imaged if the amount of movement is below a predetermined threshold,

wherein the processor is further configured to determine that at least one of the plurality of wells has two observation points in an event both of the samples included within the at least one of the plurality of wells have a visual activity greater than a predetermined threshold.

7. The measuring apparatus of claim **1**, wherein the processor is configured to determine which of the plurality of samples is to be imaged based on an input from a user.

8. The measuring apparatus of claim **1**, further comprising a vibration isolation table configured to prevent vibrations external to the measuring apparatus from being transmitted to at least one of the stage or the image device.

9. A method of measuring at least one sample included within respective wells of a vessel, the method comprising:

determining an observation position for each of the plurality of samples;

determining which of the plurality of samples is to be imaged by an image device, wherein determining which of the plurality of samples to be imaged includes determining at least one movement vector from portions of the sample within the respective well by comparing previous images of the portions of sample in the well, and determining the sample is not to be further imaged if an average of the at least one movement vector for each of the portions is below a predetermined threshold; and

imaging the samples determined to be imaged using the image device.

10. The method of claim **9**, further comprising:

determining which of the plurality of samples is not to be imaged by the image device; and

refraining from imaging the samples that are not to be imaged.

11. The method of claim **9**, wherein determining the observation positions includes:

determining coordinates of wells at four corners of the vessel;

determining a number of rows and columns of wells within the vessel;

calculating coordinates for each of the wells based on the known locations of the wells at the four corners and the number of rows and columns of the vessel; and

identifying a portion of each well as the observation position where the respective sample is visually active above a predetermined threshold.

12. The method of claim **11**, wherein the coordinates of the wells at the four corners and the number of rows and columns are provided by a user responsive to a prompt.

13. The method of claim **9**, wherein determining which of the plurality of samples to be imaged includes receiving an indication from a user.

14. The method of claim **9**, further comprising moving a stage holding the vessel or the image device to align the image device with the at least one sample that has been determined to be imaged.

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